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NEWS 10 JUN 02 The first reclassification of IPC codes now complete in
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NEWS 11 JUN 26 TULSA/TULSA2 reloaded and enhanced with new search and
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NEWS 17 AUG 28 ADISCTI Reloaded and Enhanced
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NEWS EXPRESS JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

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NEWS LOGIN Welcome Banner and News Items
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Enter NEWS followed by the item number or name to see news on that
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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 18:02:52 ON 30 AUG 2006

=> file medline, uspatful, dgene, embase, wpids, fsta, jicst, hcaplus,
COST IN U.S. DOLLARS
SINCE FILE TOTAL
ENTRY SESSION

FULL ESTIMATED COST

1.05

1.05

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```
=> s screening method
    3 FILES SEARCHED...
L1      51826 SCREENING METHOD
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=> s l1 and (protein target)
    3 FILES SEARCHED...
L2      300 L1 AND (PROTEIN TARGET)
```

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=> s l2 and (methotrexate)
L3      81 L2 AND (METHOTREXATE)
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=> s l3 and (methotrexate analog)
UNMATCHED LEFT PARENTHESIS 'AND (METHOTREXA'
The number of right parentheses in a query must be equal to the
number of left parentheses.
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=> s l3 and (methotrexate analog)
L4      1 L3 AND (METHOTREXATE ANALOG)
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=> d l4 ti abs ibib tot
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L4  ANSWER 1 OF 1  WPIDS  COPYRIGHT 2006 THE THOMSON CORP on STN
TI  New enzyme-cleavable conjugates comprising two receptor ligands useful in
    assays for screening proteins for the ability to catalyze bond cleavage.
AN  2002-147150 [19]  WPIDS
CR  2001-514515 [56]; 2004-440220 [41]
AB  US2002004202 A UPAB: 20040629
    NOVELTY - Enzyme-cleavable conjugates (I) comprising two receptor ligands
    are new.
        DETAILED DESCRIPTION - Conjugates of formula (I) are new:
        H1-X-B'-Y-H2      (I)
        H1, H2 = ligands capable of binding to the same or different
        receptors;
        X, Y = spacer groups or are absent; and
        B' = an enzyme-cleavable group.
        INDEPENDENT CLAIMS are also included for the following:
```

- (1) conjugates of formula (II):
- (2) complexes comprising (I) or (II) complexed to an enzyme;
- (3) compositions comprising both (I) and (II);
- (4) a method for screening proteins for the ability to catalyze bond cleavage, comprising:
 - (a) providing a cell that expresses a pair of fusion proteins which upon dimerization change a cellular readout;
 - (b) contacting the cell with a conjugate which dimerizes the pair of fusion proteins and comprises two portions coupled by a bond that is cleavable by the protein to be screened; and
 - (c) detecting any change in the cellular readout;
- (5) a method for screening proteins for the ability to catalyze bond formation, comprising:
 - (a) providing a cell that expresses a pair of fusion proteins which upon dimerization change a cellular readout;
 - (b) contacting the cell with two compounds, each of which is capable of bonding to one of the fusion proteins and comprises a portion through which the compounds are coupled by the action of the protein to be screened; and
 - (c) detecting any change in the cellular readout;
- (6) a method for screening a compound for the ability to inhibit an enzyme, comprising:
 - (a) screening for activity of the enzyme by method (4) or (5) to obtain cells that express an active enzyme; and
 - (b) contacting the cells with the compound to be screened;
- (7) an enzyme-inhibiting drug selected by method (6);
- (8) a method for evolving a protein with a new catalytic activity, comprising using method (4) or (5) to screen proteins from a library of proteins that are mutants of a known protein;
- (9) a protein with a new catalytic activity evolved by method (8);
- (10) a method for evolving an enzyme with a new substrate specificity, comprising using method (4) or (5) to screen enzymes from a library of enzymes that are mutants of an enzyme with known substrate specificity;
- (11) an engineered enzyme with a new substrate specificity evolved by method (10);
- (12) a method for evolving an enzyme that functions with a different cofactor from that of the corresponding natural enzyme, comprising:
 - (a) evolving mutants of the natural enzyme; and
 - (b) using method (4) or (5) to screen the mutants in the presence of a cofactor different from that of the natural enzyme;
- (13) an engineered enzyme evolved by method (12);
- (14) conjugates of formula (III):
- (15) complexes of (III) and fusion proteins comprising a methotrexate binding domain;
- (16) cells comprising the complexes of (15);
- (17) a method for dimerizing two fusion proteins inside a cell, comprising contacting the cell with a conjugate (III) in which H1 binds to one of the proteins and H2 binds to the other;
- (18) a method for identifying a molecule that binds a known target in a cell, comprising:
 - (a) covalently bonding each molecule in a pool of candidate molecules to methotrexate or a methotrexate analog to form screening molecules;
 - (b) introducing the screening molecules into cells that express a fusion protein with a methotrexate binding domain, a fusion protein comprising the known target, and a reporter gene whose expression is conditional on the proximity of the two fusion proteins;
 - (c) permitting the screening molecules to bind to the fusion proteins so as to activate expression of the reporter gene;
 - (d) selecting any cell in which the reporter gene is expressed; and
 - (e) identifying the molecule that binds the known target;
- (19) a method for identifying a protein target to which a molecule is capable of binding, comprising:

(a) providing a screening molecule comprising methotrexate or a methotrexate analog covalently bonded to a ligand with specificity for an unknown protein target;

(b) introducing the screening molecule into a cell that expresses a fusion protein with a methotrexate binding domain, a fusion protein comprising the unknown protein target, and a reporter gene whose expression is conditional on the proximity of the two fusion proteins;

(c) permitting the screening molecules to bind to the fusion proteins so as to activate expression of the reporter gene;

(d) selecting any cell in which the reporter gene is expressed; and

(e) identifying the unknown protein target.

H1-X-B'' (II) H1-Y-H2 (III)

B'' = a molecule capable of binding to an enzyme.

H1 = methotrexate or a methotrexate analog;

H2 = a ligand capable of binding to a receptor; and

Y = a covalent bond or linker.

USE - (I) in which H1 and H2 are molecules capable of dimerizing fusion proteins are useful in a method for screening proteins for the ability to catalyze bond cleavage, comprising providing a cell that expresses a pair of fusion proteins which upon dimerization change a cellular readout, contacting the cell with (I), and detecting any change in the cellular readout.

Dwg.11/20

ACCESSION NUMBER: 2002-147150 [19] WPIDS
CROSS REFERENCE: 2001-514515 [56]; 2004-440220 [41]
DOC. NO. CPI: C2002-045569
TITLE: New enzyme-cleavable conjugates comprising two receptor ligands useful in assays for screening proteins for the ability to catalyze bond cleavage.
DERWENT CLASS: B05 D16
INVENTOR(S): CORNISH, V W
PATENT ASSIGNEE(S): (CORN-I) CORNISH V W
COUNTRY COUNT: 1
PATENT INFORMATION:

| PATENT NO | KIND | DATE | WEEK | LA | PG |
|---------------|------|----------|-----------|----|----|
| US 2002004202 | A1 | 20020110 | (200219)* | | 48 |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---------------|-----------|----------------|----------|
| US 2002004202 | A1 CIP of | US 2000-490320 | 20000124 |
| | | US 2001-768479 | 20010124 |

PRIORITY APPLN. INFO: US 2001-768479 20010124; US
2000-490320 20000124

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FILE 'MEDLINE, USPATFULL, DGENE, EMBASE, WPIDS, FSTA, JICST-EPLUS, HCAPLUS' ENTERED AT 18:05:55 ON 30 AUG 2006

L1 51826 S SCREENING METHOD
L2 300 S L1 AND (PROTEIN TARGET)
L3 81 S L2 AND (METHOTREXATE)
L4 1 S L3 AND (METHOTREXATE ANALOG)

=> e cornish,v/au

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|-----|-------|----------------------|
| E1 | 1 | CORNISH WILLIAM G/AU |
| E2 | 1 | CORNISH ZIRKER D/AU |
| E3 | 0 --> | CORNISH,V/AU |
| E4 | 1 | CORNISK ERIC H/AU |
| E5 | 1 | CORNISKEY B/AU |
| E6 | 1 | CORNIST K L/AU |
| E7 | 1 | CORNIST KIM LAMAR/AU |
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